IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

WEITSCHIES, Werner et al. Examiner: DO, Pensee T.

Serial No.: 08/894,767 Group Art Unit: 1641

Filed: 2/23/1998

Title: PROCESS AND COMPOUNDS FOR DETECTION OF ANALYTES USING REMANENCE MEASUREMENT, AND USE THEREOF

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir.

The following schedule of claims reflects the Examiner's Amendment, and the correction of claim dependencies previously discussed.

This listing of claims will replace all prior versions, and listings, of claims in the application:

In the Claims:

1. **(Previously Presented)** A process for qualitative and/or quantitative detection of analytes in a liquid and/or solid phase homogeneous immunoassay, comprising determining remanence magnetization in said homogeneous immunoassay of a stable or quasi-stable ferromagnetic or ferrimagnetic substance bound to said analyte, wherein said homogenous immunoassay has been contacted with said ferromagnetic substance, whereby said substance binds to the analyte, and the presence of such magnetization is indicative of the presence or amount of the analyte.

26
2. **(Previously Presented)** A process for qualitative and/or quantitative detection of analytes in homogeneous immunoassays comprising measuring remenance magnetization of magnetic markers in a sample, bound to said analytes, wherein said homogenous immunoassay has been contacted with said ferromagnetic substance, whereby said substance binds to the analyte, and at the time of measurement the magnetization of unbound magnetic markers that are present in the sample in their totality fades owing to extrinsic superparamagnetism, and the presence of remenance magnetization is indicative of the presence or amount of said analytes.

27
3. **(Previously Presented)** A process for qualitative and/or quantitative detection of analytes in a liquid or solid phase homogeneous immunoassay, comprising

(i) labeling first structure-specific substances, with ferrimagnetic or ferromagnetic substances to indicate the presence or amount of said analyte,

(ii) adding said magnetic labeled structure-specific substances to a sample that is to be measured,

(iii) magnetizing the sample to be measured with the aid of a magnetic field or suitable intensity that is applied from outside and,

(iv) measuring the remanence of the magnetization of bound structure-specific substances with the aid of magnetic field sensors after the external field is shut off, without removing unbound structure-specific substances.

4. **(Canceled)**

23 22

5. **(Previously Presented)** The process according to claim 4, wherein the structure-specific substances are antibodies, antibody fragments, biotin, substances that bind specifically to biotin, agonists that bind specifically to receptors of their antagonists, peptides, proteins, receptors, enzyme substrates, nucleotides, ribonucleic, acids, deoxyribonucleic acids, carbohydrates, or lipoproteins.

28 27

6. **(Previously Presented)** The process according to claim 3, wherein the structure-specific substances have a binding constant in the range of 10^5-10^{15} $(mol/l)^{-1}$.

29 27

7. **(Previously Presented)** The process according to claim 3, wherein the structure-specific substances have a binding constant in the range of 10^7-10^{15} $(mol/l)^{-1}$.

2

8. **(Previously Presented)** The process according to claim 1, wherein the sample is moved during the measurement and a sample signal is modulated.

3

9. **(Previously Presented)** The process according to claim 1, wherein induction coils that are hooked up as gradiometers, fluxgate-magnetometers, giant magnetoresistance sensors, or magnetoresistive converters are used as magnetic field sensors to determine remanent magnetization.

4

10. **(Previously Presented)** The process according to claim 1, wherein SQUIDs are used as magnetic field sensors to determine remanent magnetization.

5

11. **(Previously Presented)** The process according to claim 1, wherein simultaneous determination of several different analytes in a sample of liquids or solid substances is carried out by sequential magnetization of a sample to be measured.

6 5

12. **(Previously Presented)** The process according to claim 11, wherein for simultaneous quantitative determination of analytes, different ferromagnetic or ferrimagnetic substances with discrete coercive field intensities are used.

8
~~13~~. **(Previously Presented)** The process according to claim 1, wherein the ferromagnetic and ferrimagnetic substances used have intrinsic Neelian relaxation times greater than the measuring time.

9 8
~~14~~. **(Previously Presented)** The process according to claim ~~13~~, wherein the ferromagnetic and ferrimagnetic substances that are used have Neelian relaxation times longer than 10^{-4} seconds at 20°C.

10 8
~~15~~. **(Previously Presented)** The process according to claim ~~13~~, wherein the ferromagnetic and ferrimagnetic substances that are used have Neelian relaxation times longer than 1 second at 20°C.

11
~~16~~. **(Previously Presented)** The process according to claim 1, wherein the ferromagnetic and ferrimagnetic substances have a particle size of 1 to 1000 nm.

12
~~17~~. **(Previously Presented)** The process according to claim 1, wherein the ferromagnetic and ferrimagnetic substances have a particle size in the range of 2 to 500 nm.

13
~~18~~. **(Previously Presented)** The process according to claim 1, wherein the ferromagnetic and ferrimagnetic substances are stabilized with a shell of oligomeric or polymeric carbohydrates, proteins, peptides, nucleotides, surfactants, synthetic polymers, and/or lipids.

19. **Canceled**

20. **Canceled**

21. **Canceled**

30 27

~~22.~~ **(Previously Presented)** The process according to claim ~~3~~, wherein the structure-specific substances are cytokines, lymphokines, endothelins or their antagonists.

14

~~23.~~ **(Previously Presented)** The process according to claim 1, wherein the ferromagnetic or ferrimagnetic substances are stable or quasi-stable colloidal particles that are made of iron oxides, barium ferrite, strontium ferrite, pure iron, chromium, dioxide, nickel, and cobalt, or iron oxides with manganese, copper, nickel, or cobalt additives.

7 5

~~24.~~ **(Previously Presented)** The process according to claim ~~1~~, wherein several ferromagnetic or ferrimagnetic substances with various coercive field intensities are used.

15

~~25.~~ **(Previously Presented)** In a fertility, histocompatibility, allergology, infectiology, hygiene, genetics, virology, bacteriology, toxicology, pathology, environmental analysis, or medical diagnosis process comprising detecting an analyte, the improvement wherein the detecting is performed according to claim 1.

16

~~26.~~ **(Previously Presented)** The process according to claim 1, wherein ferromagnetic or ferromagnetic substances are introduced into the human body or are applied on the human body, and the remanence of the magnetization of the ferromagnetic or ferromagnetic substances is determined after a magnetizing field is shut off.

31 27

~~27.~~ **(Previously Presented)** The process according to claim ~~3~~, wherein ferromagnetic or ferromagnetic substances are introduced into an organism or applied on the organism, by a process comprising

(i) labeling structure-specific substances with ferromagnetic or ferromagnetic substances,

(ii) adding said magnetic labeled structure-specific substances to a living organism or applied to an organism,

(iii) magnetizing a volume of the organism with the aid of a magnetic field that is applied from the outside and,

(iv) measuring remanence of the magnetic markers with the aid of magnetic field sensors after the external field is shut off.

32 31

28. **(Previously Presented)** The process according to claim 27, wherein antibodies, antibody fragments, agonists that bind specifically to receptors or their antagonists, peptides, proteins, receptors, enzymes, enzyme substrates, nucleotides, ribonucleic acids, deoxyribonucleic acids, carbohydrates, or lipoproteins are used as structure-specific substances.

33 32

29. **(Previously Presented)** The process according to claim 28, wherein the agonists or antagonists that bind specifically to receptors are cytokines, lymphokines, endothelines or their antagonists.

34 32

30. **(Previously Presented)** The process according to claim 28, wherein the structure-specific substances have a binding constant in the range of 10^5-10^{15} $(mol/1)^{-1}$.

35 32

31. **(Previously Presented)** The process according to claim 28, wherein the structure-specific substances have a binding constant in the range of 10^7-10^{15} $(mol/1)^{-1}$.

17 16

32. **(Previously Presented)** The process according to claim 26, wherein Superconducting Quantum Interference Devices (SQUIDs), induction coils, fluxgate-magnetometers, giant magnetoresistance sensors, or magnetoresistive converters are used as magnetic field sensors.

33. **Canceled**

34. **Canceled**

36 31
35. **(Previously Presented)** The process according to claim 27, wherein a mixture of different ferrimagnetic or ferromagnetic substances with structure-specific substances is used.

18 16
36. **(Previously Presented)** The process according to claim 26, wherein the Neelian relaxation time of the ferromagnetic or ferrimagnetic substances is longer than 10^{-4} second at 37°C.

20 16
37. **(Previously Presented)** The process according to claim 26, wherein the Neelian relaxation time of the ferromagnetic or ferrimagnetic substances is longer than 1 second at 37°C.

19 18
38. **(Previously Presented)** The process according to claim 36, wherein the ferrimagnetic or ferromagnetic substances are iron oxides or iron oxides with manganese, copper, nickel, or cobalt additives.

21
39. **(Previously Presented)** The process according to claim 1, wherein the ferromagnetic or ferromagnetic substance is magnetic-labeled anticollagen II and SQUID(s) are used to determine remanent magnetization.

22
40. **(Previously Presented)** A process according to claim 1, wherein the ferromagnetic or ferrimagnetic substances are used to label structure specific substances, which are added to the analyte.

24
41. **(Previously Presented)** A process according to claim 1, wherein the analyte is labeled with structure specific substances, and the ferromagnetic or ferrimagnetic substances are added thereto.

25 24

42. **(Previously Presented)** A process according to claim 41, wherein the structure-specific substances are antibodies, antibody fragments, biotin, substances that bind specifically to biotin, agonists that bind specifically to receptors of their antagonists, peptides, proteins, receptors, enzyme substrates, nucleotides, ribonucleic, acids, deoxyribonucleic acids, carbohydrates, or lipoproteins.